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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,443	06/20/2005	Anders Nykiaer	NYKJAER1	6823

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EXAMINER	
MACFARLANE, STACEY NEE	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
10/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,443	NYKIAER ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7,10,11,13-25,27-37,40-45 and 70* is/are pending in the application.

4a) Of the above claim(s) *18-25,27-32,43,44 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7,10, 11 13-17,33-37, 40-42 and 45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :12/01/2005; 2/6/2006; 11/16/2006; 3/26/2007.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 10, and the species: NGF; Sortilin and "injury and/or dysfunction of the central and/or peripheral nervous system", in the reply filed on October 4, 2007 is acknowledged. The traversal is on the ground(s) that the Jacobsen reference does not hold for a posteriori showing of lack of unity because it does not teach the inventive concept of treatment of disease. This is not found persuasive for the reasons as follows:

Pursuant to 37 C.F.R. § 1.475 (a), Unity of invention before the International Searching Authority, an international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. As such, pursuant to 37 C.F.R. § 1.475 (b), the ISA/US considers that when an international or a national stage application containing claims to different categories of invention unity of invention exists if the claims are drawn only to one of the following combinations of categories:

(1) A product and a process specially adapted for the manufacture of said product; or

(2) A product and process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

On page 1-2 of Remarks filed October 4, 2007, Applicant states that the inventions of Groups 1-11 are drawn to methods of treatment differentiated by the use of materially different therapeutic agents. Groups 12-15 are drawn to screening methods, Group 16 is a method of isolating a compound and, lastly, Groups 17 and 18 are drawn two product for use in the methods of treatment. These inventions are patentably different categories that do not fall into one of the combinations that the ISA/US considers as supporting unity of invention.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 18-25, 27-32, 43-44 and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 4, 2007.

3. Claims 1-5, 7, 10-11, 13-17, 33-37, 40-42 and 45, in so far as they are drawn to a method of treatment of disease comprising administering an effective amount of an agent; wherein the agent is an antibody directed against a sequence of SEQ ID NO: 1, will be considered upon their merits in the instant Office Action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-5, 7, 10-17, 33-37, 40-42 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. The term "modulating the activity" in claim 1 is a relative term which renders the claim indefinite. The term "modulating" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Likewise, the term “decrease” in claim 3 and “increase” in claim 4 render these claims indefinite, absent a standard for ascertaining the requisite degree, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

7. Regarding claims 1, 14 and 15, the phrase "capable of" renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

8. Claims 2-5, 7, 10-14, 16-17, 33-37, 40-42 and 45 are indefinite because they depend from indefinite claims.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 10-16, 33-37, 40-42 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

Claim 1 recites "an agent". Claims 2-5, 7, 10-16, 33-37, 40-42 and 45 are dependent from Claim 1 and do not further limit the "agent", and are therefore included in the rejection. The claims do not require that the "agent" possess any particular conserved structure or other disclosed distinguishing feature. Thus the claims are drawn to a genus of molecules that is defined only as "capable of (i) binding to a receptor of the Vps10p-domain receptor family and/or (ii) interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin and/or (iii) modulating the expression of the receptor", therefore the genus is merely defined by function and the instant specification fails to describe the entire genus of molecules that are encompassed by these claims.

In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification (Figures 2-7), it is clear that Applicant knows of specific examples of agents that mediate said effects. The claims, however, encompass method of administration of any "agent", as defined as "proteins, peptides, polypeptides, antibodies, antisense-RNA, antisense-DNA, siRNA, other polynucleotides, or organic

molecules" (page 26). Thus, the claims are not limited to specific molecules with known structure. The claims merely require the claimed methods employ molecules mediate the effects as claimed.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claim is a recitation of prospective activity. There is not even identification of any particular portion of the structure that must be conserved for said activity. As stated above, it is not even clear what molecules except NGF, ProNGF, RAP, BDNF or ProBDNF act as "agents" which mediate binding to a receptor of the Vps10p-domain receptor family and/or interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin and/or modulating the expression of the receptor. These agents are all proteins, and the claims encompass agents of different classes (i.e. antibodies and organic molecules). The specification does not provide a complete structure of these agents and fails to provide a representative number of species for the recited genus. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, the court clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of "agents" claimed, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identifying activity. Adequate written description requires more than a mere recitation of activity as part of the invention and a reference to a potential method of isolating or screening. The compound itself is required. See *Fiers v Revel*, 25 USPQ2d 1601 at 1601 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification only provided for the bovine sequence.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

10. Claims 1-5, 7, 10-17, 33-37, 40-42 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-5, 7, 10-17, 33-37, 40-42 and 45 broadly encompass methods of treatment of a disease or disorder comprising administering to an organism an effective amount of an agent capable of (i) binding to a receptor of the Vps10p-domain receptor family and/or (ii) interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin and/or (iii) modulating the expression of the receptor. These are methods that are not obvious variants of one another, for example, agents that bind the receptor do not necessarily modulate the expression of said receptor. Therefore, the claims are broadly drawn to methods comprising administering a broad range of therapeutic agents. Furthermore, the claims are broadly drawn to treatment of any disease or disorder.

The invention is based on hypothesis that modulation of the Vps10p-domain receptor family affects neurotrophin or pro-neurothrophin activity. However, the instant specification does not disclose any direct connection between Vps10p-domain receptors and neurotrophin or pro-neurothrophin activity, and therefore, is not found to be enabled for the method as claimed, for the following reasons. The instant specification does not provide evidence of a nexus between any disease/disorder and agents that (i) binding to a receptor of the Vps10p-domain receptor family and/or (ii)

interfering with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin and/or (iii) modulating the expression of the receptor. Nor does the specification provide enough guidance or working examples for methods of treating diseases or disorders comprising administering said agents, which would show that the claimed method was successfully achieved. Absent such guidance, one of ordinary skill in the art would require undue experimentation to discover how to practice Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention relates to methods of treatment for *any* disease or disorder comprising administering any agent that (i) binds to a receptor of the Vps10p-domain receptor family, (ii) interferes with binding between a receptor of the Vps10p-domain receptor family and a neurotrophin and/or proneurotrophin and/or (iii) modulates the expression of the receptor. On page 26 of the instant specification, said agents are defined as encompassing proteins, peptides, polypeptides, antibodies, antisense-RNA, antisense-DNA, siRNA, other polynucleotides or organic molecules.

On page 4 of the instant specification, Applicant states "some progress has been made as to an understanding of the role of this family [of receptors]". The following

reference indicates that at the time of filing, the state of the art with respect to a function of these receptors was speculative at best (J. Mazella, Cellular Signalling, 13:1-6, January 2001). Figure 2 (page 4) of the Mazella reference depicts many possible functions of the sortilin/NTR3 but defines no clear roles. Furthermore, the reference teaches that very little of sortilin/NTR3 is expressed at the cell surface (page 4, lines7-10) indicating that the any role for this receptor in neuropeptide signaling is "essentially intracellular" (page 5, lines 9-11).

With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the scope of enablement, the claims are analyzed with respect to the teachings of the specification and are to be given their broadest reasonable interpretation that is consistent with the specification. See MPEP 2111 [R-1], which states: "During patent examination, the pending claims must be "given *>their< broadest reasonable interpretation consistent with the specification." *In re Hyatt*, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

As such, the broadest reasonable interpretation of the claimed method is that it allows for the treatment of *any* disease/disorder comprising administering *any* agent that mediates *any* of the following effects: binding to receptor, interfering with binding, or

modulating expression of the receptor. Thus, the claims encompass an unreasonable number of pathologically distinct conditions and disorders, many of which have no nexus or association at all to Vps10p-domain receptor binding or expression. A skilled artisan would not know how to treat these diseases based solely on administration of an agent that mediates said effects. As opposed to the claims, what is disclosed about the claimed method is narrow: There are no working examples of any agent that is known to mediate such effects, and no guidance or direction as how to make and use said agents with a reasonable expectation of success to practice the full scope of treatment of disease/disorder. Therefore, the disclosure provides no guidance as to how to make and use the invention to the full extent of the scope claimed.

Claims 1 is a single means claims in that it recites "an agent", which is defined in "modulating the activity of at least one neurotrophin". MPEP 2164.08(a) defines a single means claim as a claim which covered every conceivable means for achieving the stated purpose when the specification disclosed at most only those means known to the inventor. This type of claim was held to be nonenabling for the scope of the claim in *In re Hyatt*, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983) because the specification disclosed at most only those means known to the inventor. When claims depend on a recited property (i.e. modulating), a fact situation comparable to Hyatt is possible, where the claim covers every conceivable structure (means) for achieving the stated property (result) while the specification discloses at most only those known to the inventor. This appears to be the instant case and Applicant should note that the claims encompass the administration of *any* drug due to the definition of "agent" in the specification.

While the skill level in the art is high, the level of predictability is low. Although the agent of the claims can broadly encompass proteins, peptides, polypeptides, antisense-RNA, antisense-DNA, siRNA, other polynucleotides or organic molecules, the preferred embodiment is the instantly elected antibody directed against a peptide comprising amino acids 612-740 of SEQ ID NO: 1, which encodes sortilin (specification page 8). The instant disclosure provides no guidance or evidence that the administration of said antibody mediates the claimed effects upon intracellular receptors, let alone treats a disease. Furthermore, in the Paper filed October 4, 2007, Applicant has elected the specific treatment of "injury and/or dysfunction of the central and/or peripheral nervous system". As the following current reference indicates, "Essentially 100% of all large molecule drugs do not cross the [blood brain barrier], including all of the products of biotechnology: recombinant proteins and enzymes, monoclonal antibodies (MAb), antisense drugs, short interfering RNA (siRNA), or gene therapy" (page 1733, paragraph 2 from W.M. Pardridge, Pharmaceutical Research 24(9): 1733-1744, September 2007).

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

Conclusion

11. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on M,W and ALT. F 6 am to 3 pm, T & R 5:30 am - 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
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/SNM/

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PRIMARY EXAMINER